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Spiegel et al.(10) **Pub. No.: US 2021/0284988 A1**(43) **Pub. Date: Sep. 16, 2021**(54) **REPROGRAMMING UROKINASE INTO AN
ANTIBODY-RECRUITING ANTICANCER
AGENT***A61K 47/54* (2006.01)*A61K 31/352* (2006.01)*A61K 38/05* (2006.01)*A61K 38/48* (2006.01)(71) Applicant: **YALE UNIVERSITY**, NEW HAVEN,
CT (US)*C07D 491/107* (2006.01)*C07K 5/062* (2006.01)(72) Inventors: **David A. Spiegel**, New Haven, CT
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Worcester, MA (US)(52) **U.S. Cl.**CPC *C12N 9/96* (2013.01); *A61K 45/06*(2013.01); *C07D 493/10* (2013.01); *A61K**31/165* (2013.01); *A61K 31/365* (2013.01);*C07C 279/12* (2013.01); *C07K 5/06026*(2013.01); *A61K 47/54* (2017.08); *A61K**31/352* (2013.01); *A61K 38/05* (2013.01);*A61K 38/482* (2013.01); *C07D 491/107*(2013.01); *A61K 47/60* (2017.08)(21) Appl. No.: **17/182,437**(22) Filed: **Feb. 23, 2021****Related U.S. Application Data**(60) Division of application No. 16/149,299, filed on Oct.
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11, 2011.**Publication Classification**(51) **Int. Cl.***C12N 9/96* (2006.01)*A61K 45/06* (2006.01)*C07D 493/10* (2006.01)*A61K 31/165* (2006.01)*A61K 31/365* (2006.01)*C07C 279/12* (2006.01)*A61K 47/60* (2006.01)

(57)

ABSTRACT

The present invention relates to chimeric (preferably, bifunctional) compounds, compositions comprising those compounds and methods of treating cancer in a patient or subject, especially including metastatic cancer where cancer cells exhibit overexpression (heightened expression) of cell surface urokinase-type plasminogen activator receptor (urokinase receptor) compared to normal (non-cancerous) cells. The compounds preferably covalently bind to the urokinase receptor and recruit native antibodies of the patient or subject where the antibodies can selectively degrade and/or deactivate targeted cancer cells through antibody-dependent cellular phagocytosis and/or antibody-dependent cellular cytotoxicity (ADCC) against a large number and variety of cancers, thus providing cancer cell death and/or an inhibition of growth, elaboration and/or metastasis of the cancer, including remission and cure of the patient's cancer.